

REMARKS

Claims 1, 2, 4-7, 10, 12, 14, 15, 17-19, 23, 24, 26 and 30 are pending. Of these, claims 4 and 30 have been allowed.

For the convenience of the Examiner, the following exhibits are attached hereto:

Exhibit A: Second Declaration of Dr. Steven J. Saul

Exhibit B: Childs et al., US Patent 5,783,399, issued July 21, 1998

Interview Summary

Applicants wish to thank the Examiner for participating in the telephone interview held on June 28, 2005, with Mr. Richard Long, Esq. of Charm Sciences Inc., and the undersigned representative.

¶6: Rejection under 35 U.S.C. § 103(a): Bernstein in view of Simpson and Rich

Claims 1, 2, 5-7, 10 and 12 have been rejected under 35 U.S.C. § 103(a) as not being patentable over Bernstein (US 4,770,853; "Bernstein") in view of Simpson et al. (EP 0 309 184; "Simpson") and Rich et al. (US 3,666,631; "Rich"). The rejection is respectfully traversed.

The examiner must establish factual basis for obviousness to a preponderance of the evidence, by determining the scope and content of the prior art, identifying the differences between the prior art and the claimed invention as a whole, determining the level of skill in the art, and providing factual support for finding a greater than 50% likelihood that one of ordinary skill in the art would not merely have been motivated to solve the problem, but be motivated to arrive at the same solution as that claimed.

The examiner has not met that burden. First, the examiner has not taken all claim limitations into account, and thus has not considered the invention as a whole. Second, as demonstrated by the Second Declaration of Steven J. Saul (Exhibit A) and the Childs et al. patent (Exhibit B hereto), it has not been established to a preponderance of the evidence that that the skilled artisan would find a suggestion or motivation in the references to modify the Bernstein apparatus according to the disclosures of Simpson and Rich. As testified to by Dr. Saul, one of ordinary skill in the art in 1995, reading the Bernstein, Simpson, and Rich patents,

would not have been motivated to provide a unit dose reagent chamber containing a luciferin-luciferase reagent by placing luciferin-luciferase in the vessel of the Bernstein apparatus, because the Bernstein apparatus is not suitable for chemiluminescent detection of ATP, and because modification of the Bernstein apparatus for chemiluminescent detection of ATP would have made the Bernstein apparatus unsuitable for its intended purpose of a solid phase immunodiffusion assay. Dr. Saul further testifies that one of ordinary skill in the art in 1995, reading the Bernstein, Simpson, and Rich patents, would not have been motivated to provide a unit dose reagent chamber containing a detergent-containing buffered solution for use in a test apparatus for detecting ATP in a test sample, by placing a detergent-containing buffered solution in the vessel of the Bernstein apparatus. The Bernstein apparatus features an open portal window and relies for its operation on the presence of a prefilter and capture membrane, and thus would not be suitable for use in ATP detection. Modification of the Bernstein apparatus to be suitable for ATP detection, by the substantial reconstruction of eliminating the prefilter and capture membrane, would result in leakage of unabsorbed fluid out of the window.

Finally, the Childs patent is relevant as a secondary consideration of non-obviousness. *Monarch Knitting Machinery Corp. v. Sulzer Morat GmbH*, 139 F.3d 877, 45 U.S.P.Q.2d 1977, 1983 (Fed.Cir. 1998) (“*Therefore, this court will address the evidence of contemporaneous invention in that context.*”). The Childs patent demonstrates that others of ordinary skill in the art in 1995, seeking to provide a device for chemiluminescent detection of detergent-released ATP in a test sample and in similar possession of Bernstein, Simpson, and Rich, were *not* motivated to provide a unit dose reagent chamber for ATP detection containing a detergent-containing buffered solution or a luciferin-luciferase reagent. Childs et al. arrived at a completely different solution than that of the claimed invention. Evidence in the form of the Childs patent reduces the likelihood that one skilled in the art would be motivated by the references to arrive at the claimed invention to below 50%. The rejection can not be maintained.

Differences between the claimed invention and the prior art

The first step of an obviousness determination is to identify all the differences between the claimed invention and the teachings of the prior art. All words in applicant’s claim must be considered in judging the patentability of that claim against the prior art. MPEP 2143.03 (citing *In re Wilson*, 424 F2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970))(reversing Board’s

finding of obviousness where Board ignored language in the claim). The invention is defined by claim 1 (emphasis added):

1. A unit dose reagent chamber *for use in a test apparatus for the detection of adenosine triphosphate (ATP)* in a test sample, and wherein a moveable probe is employed to obtain a test sample *and to release reagents from the reagent chamber to a test unit*, which unit dose chamber comprises:
 - a) a cylinder having a one open end and an other opposite open end;
 - b) a probe-puncturable membrane seal over the one end and the other end of the cylinder to form a sealed compartment; and
 - c) a reagent composition within the sealed compartment, which composition consists essentially of and is selected from the group consisting of:
 - i) a detergent-containing buffered solution to release adenosine triphosphate (ATP) from the test sample into the solution for testing; and
 - ii) a luciferin-luciferase reagent.

The unit dose reagent chamber of claim 1 contains a detergent-containing buffered solution and/or a luciferin-luciferase reagent, for use in a test apparatus that would be suitable for performing an ATP detection assay that employs one or both of these reagents. To consider the invention as a whole, the rejection must account for the recitations of the preamble. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430, 1432 (Fed. Cir. 1990) (reversing Board's rejection of all claims as obvious where differences between reference and claims lie solely in the functional language in the preamble reciting an intended use for the machine).

When stating that,

[t]he reference of Bernstein discloses a unit dose reagent chamber for use in a test apparatus (See Figure 4)"

the examiner ignores crucial claim limitations, and thus does not consider the claimed invention as a whole. See, Office Action, page 4, lines 708. The proper inquiry is not whether Bernstein discloses "*a unit dose reagent chamber for use in a test apparatus*", but rather whether Bernstein discloses "*unit dose reagent chamber for use in a test apparatus for the detection of adenosine triphosphate (ATP) in a test sample*". Bernstein does not disclose a test apparatus suitable for detecting detergent-released ATP by chemiluminescent reagents.

Critical features of the Bernstein test apparatus make it decidedly unsuitable for chemiluminescent detection of ATP, and unsuitable for use in an ATP detection reaction requiring a detergent-containing buffered solution. Although the examiner acknowledges that the Bernstein test apparatus has been designed to perform an immunoassay, not to detect ATP,

the examiner asserts that column 1, lines 13-28, and column 3, lines 11-28 support a broader interpretation of Bernstein. Office Action, page 4, lines 15-19. The cited passages are inconsistent with that assertion. Column 1, lines 13-28, is a general background statement of a problem to be solved in the art relating to using analyte detection in diagnostic tests. Column 3, lines 11-28, is a generalized list of reagents that Bernstein discloses to be suitable for use in conjunction with the Bernstein test apparatus. The list omits any specific suggestion of reagents useful for chemiluminescent detection of ATP. Neither of these general statements broaden the scope of suitability of Bernstein's test apparatus to chemiluminescent detection of detergent-released ATP.

The examiner attempts to explain why the identified differences would have been the result of an obvious modification of the prior art as follows:

In view of these teachings, it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide the adenosine triphosphate detection reagents as taught by the prior art references of Simpson et al. and Rich et al. within the test device structure as disclosed by the reference of Bernstein for the known and expected result of employing an alternative means recognized in the art for storing and performing a multiple step assay while providing the benefits disclosed by the reference of Bernstein when using the disclosed reagent holding system (See column 1, lines 4-28).

Office Action, page 5, lines 6-12 (emphasis added). Column 1, lines 4-28, of Bernstein is nothing more than a background discussion articulating the problem of providing rapid diagnostic assays having multiple steps, multiple reagents, and limited storage conditions. By the examiner's reasoning, one skilled in the art would have been motivated to modify the Bernstein apparatus for any multi-step assay by placing *any* reagents into the vessels of Bernstein. In taking this position, the examiner does not address the specific language of the claim 1. Focusing on the obviousness of substitutions and differences, instead of on the invention as a whole, is a legally improper way to simplify the question of obviousness. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 231 USPQ 81, 93 (Fed.Cir. 1986).

There is no suggestion or motivation to combine the cited references

The rejection should be withdrawn as lacking any rationale as to how or what would have suggested or motivated the skilled artisan to modify the Bernstein apparatus to provide the claimed invention. Merely alleging that the references can be combined or modified does not make the resulting combination obvious unless the prior art also suggests the desirability of the combination. MPEP 2143.01.

There is no motivation to combine references where, as here, the proposed modification would change the principle of operation of the prior art apparatus of the primary reference, and would render the prior art apparatus unsatisfactory for its intended purpose.

It is well established that no suggestion or motivation to combine is present where the proposed modification would change the principle of operation of the prior art reference. MPEP 2143.01 (p. 2100-132), *citing, In re Ratti*, 270 F.2d 810, 813, 123 USPQ 349, 352 (CCPA 1959) (*obviousness rejection reversed where suggested combination of references would require a substantial reconstruction and redesign of the elements shown in the primary reference as well as a change in the basic principle under which the primary reference construction was designed to operate*). It is also well established that there is no suggestion or motivation to combine the references where the proposed modification would render the prior art unsatisfactory for its intended purpose. MPEP 2143.01 (p. 2100-131), *citing, In re Gordon*, 733 F.2d 900, 221 USPQ 1124 (Fed. Cir. 1984) (BPAI's conclusion of *prima facie* obviousness reversed based on finding that, were prior art device to be turned upside down, it would have been inoperable for its intended purpose).

Bernstein is directed to an apparatus for performing a solid phase immunodiffusion assay in which a proteinaceous antibody or receptor is bound as a capture ligand to a membrane positioned over a hole at the bottom end. Bernstein operates by delivering ligand from the test sample to the capture membrane, whereby a ligand:receptor interaction is formed between the ligand and the capture agent and a signal is concentrated on the membrane sufficient to visualize the signal through a window 11. At least two objectives are fundamental to the teachings of Bernstein.

First, one of ordinary skill in the art in 1995, reading the Bernstein, Simpson, and Rich patents, would not have been motivated to provide a unit dose reagent chamber containing a

luciferin-luciferase reagent by placing luciferin-luciferase in the vessel of the Bernstein apparatus, because the Bernstein apparatus is not suitable for chemiluminescent detection of ATP, and because modification of the Bernstein apparatus for chemiluminescent detection of ATP would have made the Bernstein apparatus unsuitable for its intended purpose of a solid phase immunodiffusion assay. Second Declaration of Dr. Steven J. Saul (Exhibit A, "Saul Declaration"), ¶9. The Bernstein apparatus is designed so that assay results can be observed visually through window 11, which is a discrete observation portal on the front side of lower portion 10. (See Figs. 5 of Bernstein). In fact, Bernstein states clearly that the Bernstein apparatus is designed to operate independently of instrumentation such as scintillation counters, fluorimeters and colorimeters. Bernstein, column 1, para. 2; Saul Declaration, ¶12. To concentrate the signal in front of the window Bernstein must do four things: (a) capture the labeled members of the binding pair on capture membranes 18, 19; (b) eliminate interfering substances on a pre-filter membrane 25; (c) remove excess fluid on absorbent 17; and (d) deliver the reagents into direct proximity in front of the prefilter and reaction membranes. (See col. 5, lines 5-8: "The shape of the lower portion 10 is configured to enhance contact of the collection device tip with the pre-filter or reaction membranes.") Bernstein, column 3, lines 34-51; Saul Declaration, ¶17. Absent each of these design features, Bernstein would not be able to achieve sufficient signal enhancement for visualization through the front window 11. Saul Declaration, ¶17.

It is an indicia of nonobviousness where, as here, the suggested combination of references would require a substantial reconstruction and redesign of the elements shown in the primary reference, as well as a change in the basic principle under which the primary reference construction was designed to operate. In order to modify the Bernstein device for use with luciferin-luciferase, the Bernstein device would have had to have been adapted for chemiluminescent detection, i.e., by modifying the device to be suitable for use with a luminometer. Were the Bernstein device to have been so adapted, there would be no concentration of signal in front of window 11, and the Bernstein apparatus would then be unsatisfactory for its intended purpose. Saul Declaration, ¶¶18-20.

Second, one of ordinary skill in the art in 1995, reading the Bernstein, Simpson, and Rich patents, would not have been motivated to provide a unit dose reagent chamber containing a detergent-containing buffered solution for use in a test apparatus for detecting ATP in a test

sample, by placing a detergent-containing buffered solution in the vessel of the Bernstein apparatus. The Bernstein apparatus features an open portal window and relies for its operation on the presence of a prefilter and capture membrane, and thus would not be suitable for use in ATP detection. Modification of the Bernstein apparatus to be suitable for ATP detection, by the substantial reconstruction of eliminating the prefilter and capture membrane, would result in leakage of unabsorbed fluid out of the window. Saul Declaration, ¶10 and ¶¶20-22.

For related reasons, the examiner has not established a *prima facie* case of obviousness with respect to claims 7 and 10. The inventions of claims 7 and 10 are directed to the combination of the unit dose reagent chamber and test apparatus of claim 5, along with a closed bottom end, transparent test unit at one end of the test apparatus. The bottom end of the Bernstein device, in contrast, features a window 11, is not closed. Saul Declaration, ¶10 and ¶¶20-22; *see also*, Bernstein, claim 1, element h)(“*means forming a hole in said tube . . .*”). One skilled in the art would not be motivated to place a detergent containing buffered solution into the Bernstein apparatus. The bottom of the Bernstein device is not closed, so any solution would leak out the hole at the bottom of the test apparatus.

Secondary indicia of non-obviousness reduces the likelihood that one skilled in the art would be motivated to combine the prior art references to below the required 50% threshold..

A decision to maintain a rejection must show that the decision is based on the totality of the evidence. MPEP 2143.01. The examiner must consider not only those references cited, but also any and all evidence that supports patentability of applicant's invention, including any evidence of secondary considerations submitted by the applicant in rebuttal. *Id.* Evidence establishing a secondary indicia of non-obviousness can include evidence that others of ordinary skill in the relevant art arrived at alternative solutions. *Monarch Knitting Machinery Corp.*, 45 USPQ2d at 1983. General skepticism of those in the art that does not amount to "teaching away" is still relevant and persuasive evidence of non-obviousness. *Monarch Knitting Machinery Corp.*, 45 USPQ2d at 1984.

In the present case, there is at least a 50% likelihood that one skilled in the art, in possession of the cited references and seeking to solve the problem of detecting ATP using one or more of a detergent and a luciferin-luciferase reagent, would have chose *not* to modify the Bernstein test apparatus, but rather would have pursued an alternative solution. Evidence of the

fact that one skilled in the art was at least as likely to pursue different options is found in US Patent 5,783,399, which was filed on November 17, 1995 by inventors Mary Ann Childs, Gregory K. Shipman, William P. Trainor, Erick Gray, and David Bernstein (“Childs et al.”, Exhibit B hereto).

We do not know what actually motivated Childs et al, but even if we did it would be irrelevant to the issue of obviousness. *Amazon.com, Inc. v. Barnesandnoble.com, Inc.*, 239 F.3d 1343, 57 U.S.P.Q.2d 1747 (Fed.Cir. 2001). The relevant inquiry is what a hypothetical ordinarily skilled artisan would have gleaned from the cited references at the time of the invention. *Id.* The written disclosure of the Childs et al. patent is *prima facie* evidence establishing that it is just as likely that the skilled artisan, seeking to solve the problem of providing a device for chemiluminescent detection of detergent-released ATP in a test sample, would have arrived at a completely different solution than that encompassed by the claimed invention. Given evidence of an alternative solution by those skilled in the art in 1995, a *prima facie* case of obviousness has not been established to a preponderance of the evidence. *Monarch Knitting Machinery Corp.*, 45 USPQ2d at 1982 (reversing the district court’s finding of obviousness where “*All of these references stated the problem as preventing hook breakage at high speeds. Each of these references proposed a different solution. Thus, this evidence creates a genuine issue as to whether those of ordinary skill would have had a motivation to combine needles with varying stem segment heights to form a trend.*”).

The inventors of the Childs et al. patent sought to use chemiluminescent methods to detect ATP when monitoring surfaces for bacterial contamination. Childs et al., column 1, lines 6-56. Childs et al. recognized that luciferin-luciferase reactions of the firefly had been used previously for detecting threshold levels of microorganisms. Childs et al., paragraph bridging columns 1-2. But Childs et al. also recognized that lyophilized luciferase-luciferin reagent could be unstable at room temperature during long term storage, and considered it to be unstable after liquid reconstitution over short time intervals. *Id.*

Given that all of the cited references of Bernstein, Simpson, and Rich predated the filing date of Childs et al., applicant is entitled to the legal presumption that the cited references were constructively available to Childs et al. Yet when faced with the problem of using luciferin-luciferase to detect ATP on a test surface as an indication of bacterial contamination, the

inventors of the Childs patent did not choose to modify the Bernstein reference. The inventors on the Childs patent chose a completely different solution to that problem.

The device that Childs et al. discloses for accomplishing this goal is a lateral flow type device having a lateral flow membrane on a solid support strip, having a sample portion, a reagent portion, and a fluid reservoir on the test strip that breaks in response to finger pressure to cause carrier fluid to flow from the reservoir across the lateral flow strip. The solution arrived at by Childs et al. included either drying a detergent onto the sample portion or reagent portion of the test strip (col. 5, lines 7-10 and 61-65), or placing a detergent into the carrier fluid in the fluid reservoir (col. 3, lines 31-33 and col. 6, lines 4-5). The solution of Childs et al. further includes applying a reconstituted solution of luciferin-luciferase to the membrane filter strip and drying *in vacuo* (col. 8, lines 49-56).

Thus, the Childs et al. patent makes it clear that, despite having constructive possession of the cited references, one of skill in the art would not necessarily have arrived at the solution of providing a unit dose reagent chamber containing either a detergent-containing buffered solution or a luciferin-luciferase reagent. It has not been established to a preponderance of the evidence, i.e., that it is more than 50% likely, that one skilled in the art would have been motivated to modify or combine Bernstein, Simpson, and Rich to arrive at the unit dose reagent chamber, test apparatus, and test unit of applicant's claimed invention.

In light of the above, applicant submits that the rejection can not be maintained, because the rejection lacks rationale as to why the skilled artisan would modify the Bernstein apparatus in keeping with the disclosures of Simpson and Rich, given that such modifications would have required substantial reconstruction of the Bernstein apparatus, changed its principle of operation, and rendered it unsuitable for its intended purpose. In addition, the Childs patent is evidence that those skilled in the art, in constructive possession of the same prior art references in 1995 and seeking to solve the problem of providing a device for chemiluminescent detection of ATP in a test sample, would have been just as likely to seek a completely different solution. Thus, the totality of the evidence does not support a conclusion that there is a greater than 50% likelihood that the claimed invention would have been obvious to one skilled in the art in view of Bernstein, Simpson, and Rich. Applicant respectfully submits that the rejection should be withdrawn.

¶7: Rejection under 35 U.S.C. § 103(a): Bernstein in view of Simpson, Rich, and Matsumoto

Claims 10, 14, 15, 17-19, 23, 24 and 26 have been rejected under 35 U.S.C. § 103(a) as not being patentable over Bernstein (US 4,770,853) in view of Simpson et al. (EP 0 309 184; “Simpson”) and Rich et al. (US 3,666,631; “Rich”) and taken further in view of Matsumoto et al. (JP 7-59555). The rejection is respectfully traversed.

The Bernstein, Simpson, and Rich references have been discussed above. The above arguments and the testimony set forth in the Saul Declaration relating to the Bernstein, Simpson, and Rich references apply equally to the invention of claims 10, 14, 15, 17-19, 23, 24, and 26. In addition, Childs et al., US Patent 5,783,399 (Exhibit B) is secondary indicia that one skilled in the art, having possession of Bernstein, Simpson, Rich, and Matsumoto, would not have been motivated to arrive at the solution of the claimed invention.

All of the cited references of Bernstein, Simpson, Rich, and Matsumoto predated the filing date of Childs et al. Applicant is thus entitled to the legal presumption that the cited references were constructively available to Childs et al. Although Childs et al. sought to provide a device for detecting ATP on a test surface as an indication of bacterial contamination, the inventors of the Childs patent did not choose to modify the apparatus of the primary Bernstein reference according to the disclosures of Simpson, Rich, and Matsumoto. The inventors on the Childs patent chose a completely different solution to that problem, namely, a lateral flow diffusion assay.

Childs et al. establishes that there is at least a 50% likelihood that one skilled in the art, in possession of the cited references and seeking to solve the problem of detecting ATP using one or more of a detergent and a luciferin luciferase reagent, would have chosen *not* to modify the Bernstein test apparatus, but rather to have pursued an alternative solution. Thus, the examiner has not established that those skilled in the art, in possession of the cited references, would have necessarily arrived at the claimed invention. Other options were available. Thus, has not been established to a preponderance of the evidence, i.e., more than a 50% likelihood, that one skilled in the art would have been motivated to modify or combine Bernstein, Simpson, Rich, and Matsumoto to arrive at the combination, test apparatus, and test unit of claims 10, 14, 15, 17-19, 23, 24, and 26. Applicant respectfully requests that the rejection be withdrawn.

CONCLUSION

The present Amendment is being filed within six months of the mailing date of the Office Action, and a petition for extension of time of three months is enclosed herewith. Please charge any outstanding fees or credit any overpayments to Deposit Account No. 50-1895, Ref. No. 0656-008US6.

Respectfully submitted:

Date: 9/28/05


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Enclosures:

Exhibits A and B
Petition for Extension of Time (3 mos.)
Fee Transmittal, Postcard

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